REMARKS

Status of the claims

Claims 1-2 and 4-8 are pending in the application. Claim 3 was previously cancelled. Claims 5 and 7 are withdrawn. Claims 1, 2, 4, and 6 are amended herein. Claim 1 has been amended for clarity. Claim 2 has been amended to remove a smaller recited range that falls within a large range and claims 4 and 6 have been amended to be drawn to methods of "improving wrinkled or dry skins". Support for the amendments to claims 4 and 6 may be found at least on page 8, lines 3-7 of the specification. New claim 8 has been added and finds support in original claim 2. No new matter has been added with the amendments or new claim. As such, entry and consideration thereof are respectfully requested.

Restriction of the claims

Applicants acknowledge the rejoinder of claims 4 and 6 and continued restriction of claims 5 and 7.

Objections to the claims

Claim 2 has been objected to as being of improper form for failing to further limit claim 1. Claim 2 has been amended to recite that the molecular weight of the hyaluronate fragments is between 50,000 and 250,000 Da. As such, claim 2 further limits the scope of claim 1, which defines the molecular weight of the hyaluronate fragments as between 50,000 and 750,000 Da. Withdrawal of the objection is respectfully requested.

Rejections under 35 U.S.C.§112, 2nd paragraph

Claims 2, 4 and 6 have been rejected under 35 U.S.C.§112, 2nd paragraph as being indefinite. More specifically, the claims have been rejected for recitation of "prevention". Applicants note that this rejection is inappropriate as applied to claim 2, since claim 2 does not recite a "prevention."

With regard to claims 4 and 6, the claims have been amended to more clearly recite methods of "improving wrinkled or dried skins". Withdrawal of the rejection is therefore respectfully requested.

Rejections under 35 U.S.C.§103

Claims 1, 2, 4 and 6 have been rejected under 35 U.S.C.§130 as being obvious over Liu et al. US '956 in view of Balazs US '676. Liu et al. US '956 is asserted to teach topical compositions comprising retinol for treating wrinkles and dryness of the skin. The compositions of Liu et al. US '956 are noted for further containing hyaluronic acid for its moisture properties and also treating wrinkles. The Examiner notes that Liu et al. US '956 fails to teach the recited molecular weight of the hyaluronic acid as recited in claim 1. The Examiner pointes to Balazs et al. US '676 for curing the alleged deficiency of Liu US '956 and for teaching hyaluronic acid compositions for moisturizing skin which contain hyaluronate at 10,000 to 200,000 Da. Balazs et al. US '676 is further asserted to teach that the lower molecular weight hyaluronic acid penetrates deeper into the skin. The Examiner asserts that it would have been obvious to use formulations containing hyaluronic acid having a molecular weight of 50,000-750,000 Da to produce the compositions of the invention because Liu et al. US '956 teach hyaluronic acid used in topical skin care compositions and Balazs et al. US '676 teaches the recited molecular weight ranges to use. Applicants traverse this rejection and withdrawal thereof is respectfully requested.

The present invention, as encompassed by claim 1, is drawn to,

> Topical compositions, comprising as an active ingredient, one or more hyaluronate fragments, wherein the hyaluronate fragments all have a molecular weight of between 50,000 and 750,000 Da and at least one retinoid selected from the group consisting of retinol and isomers thereof, retinal, and esters of retinoic acid.

The Examiner considers that the difference between the subject-matter of claim 1 and the disclosure of Liu et al. US '956 is the molecular weight of the hyaluronate fragments, which is not specified in Liu et al. US '956. However, several studies have indicated that the molecular weight of hyaluronic acid can be essential to the efficacy of a composition, since the molecular weight can lead to different pharmacological effects on cells and tissues (McKee et al., 1996; Termeer et al., 2000; Fitzgerald et al., 2000; see from page 2, line 22 of the specification, copies of the references were included with the IDS filed on October 30, 2006.).

The Examiner asserts that it would be obvious for the person skilled in the art to use hyaluronate fragments having a molecular weight as claimed in view of the patent Balazs et al.

US '676. However, all of the compositions used in Balazs et al. US '676 comprise two different molecular weight hyaluronate fractions, i.e. a low molecular weight fraction, which is between 10,000 and 200,000 Da, and a high molecular weight fraction, which is between 1,000,000 and 4,500,000 Da (see notably claim 1 and col. 1, lines 64-68 of Balazs et al. US '676). Moreover, Example I of Balazs et al. US '676 shows clearly the importance of the high molecular weight fraction of hyaluronate being present (col. 4, line 1-24).

The experiment of Example 1 of Balazs et al. US '676 shows the treatment of hairless mice with "HPE" or "D-HPE". HPE corresponds to a composition which has only the high molecular weight fraction of hyaluronate having a molecular weight of 1,000,000 and 4,500,000 Da (see col. 2, lines 40-50). D-HPE, on the other hand, corresponds to HPE in which the hyaluronic acid had been broken down by heat degradation (see col. 4, lines 8-10) leading to a composition comprising only a low molecular weight faction (30,000-200,000 Da) of hyaluronate (see col. 2, lines 53-61).

Figures 1 and 2 show the surface of the mouse skin cells obtained after each of these treatments and the results clearly show that the surface of the skin is smooth after a treatment with HPE, whereas the surface of the skin has many cracks and folds after a treatment with D-HPE (see col. 4, lines 13-18).

Importantly, the only difference between HPE and D-HPE is the molecular weight of the hyaluronic acid. Thus, Balazs et al. US '676 clearly teaches the crucial role of the presence of a high molecular weight fraction (1,000,000-4,500,000 Da) of hyaluronic acid for the efficacy with a topical composition.

Thus, in view of the knowledge of Balazs et al. US '676, the person skilled in the art would be motivated to use a high molecular weight fraction (1,000,000-4,500,000 Da) of hyaluronic acid and not a hyaluronate having a molecular weight comprised between---. 50,000 and 750,000 Da. Indeed, based on the disclosure of Balazs et al. US '676, one of ordinary skill in the art would believe that the presence of high molecular weight hyaluronate is essential for efficacy.

Yet, the inventors of the present patent application have clearly demonstrated that a composition comprising a hyaluronate having a molecular weight comprised between 50,000 and 750,000 Da, in association with a retinoid, has a better biological activity than the same

composition comprising, in place of the hyaluronate fragments described previously, a hyaluronate having a molecular weight comprised between 1,000 and 20,000 Da or comprised between 1,000,000 and 2,000,000 Da (see tables 1-7). These results are completely unexpected in view of the teachings of Balazs et al. US '676, which directs one skilled in the art to the high molecular weight fraction.

Consequently, the subject-matter of the claims is not obvious over Liu et al. US '956 in combination with Balazs US '676. Withdrawal of the rejection is therefore respectfully requested.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact MaryAnne Armstrong, PhD, Registration No. 40,069 at the telephone number of the undersigned below to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Director is hereby authorized in this, concurrent, and future replies to charge any fees required during the pendency of the above-identified application or credit any overpayment to Deposit Account No. 02-2448.

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Respectfully submitted,

By _____

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